

ORAL MICROBIOTA AND SYSTEMIC DISEASES

Gayathri Ganapathy¹, Mudiyaayirakkani Muthusamy²

¹ *Private Practitioner, Erode-63815.*

² *Department of Oral Biology, Saveetha Dental College and Hospital,
Saveetha Institute of Technical and Medical Sciences, Chennai – 600 077.*

ABSTRACT

Human oral microbiota is the ecological community of commensal, symbiotic, and pathogenic microorganisms found in the oral cavity. Oral microbiota generally exists in the form of a biofilm and plays a crucial role in maintaining oral homeostasis, protecting the oral cavity and preventing disease development. Human oral microbiota has recently become a new focus research for promoting the progress of disease diagnosis, assisting disease treatment, and developing personalized medicines. In this review, the scientific evidence supporting the association that endogenous and exogenous factors (diet, smoking, drinking, socioeconomic status, antibiotics use and pregnancy) modulate oral microbiota.

Key Words: Oral microbiota, systemic diseases, pathogenesis, colonization, oral cavity.

Address for correspondence:

Dr. Mudiyaayirakkani Muthusamy

Saveetha Dental College and Hospitals, Chennai

Email: drmudiyaayirakkanimuthusamy95@gmail.com

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INTRODUCTION

The oral cavity is a connection channel between outside environments and the respiratory tract and digestive tract. It provides an appropriate temperature, humidity, and nutrition for microorganism colonisation. The disturbance of the oral microbiota– ecology balance in the host usually causes a series of oral infectious diseases including dental caries, apical periodontitis, periodontal diseases, pericoronitis, and craniofacial bone osteomyelitis. Oral microbiota is also associated with several systemic diseases, namely cardiovascular disease, pneumonia, heart disease, rheumatoid arthritis, pancreatic cancer, colorectal cancer, oesophageal cancer, stroke, and adverse pregnancy outcomes.

Basic composition and distribution of oral microbiota:

The oral microbiome can be classified into core microbiome and variable microbiome. The core microbiome is similar for all individuals and comprised of the predominant species at different sites of the healthy body⁽¹⁾. The variable microbiome is different between individuals in response to unique lifestyles and phenotypic and genotypic determinants. The oral cavity contains over 700 microbial species as well as commensal and opportunistic bacteria, archaea, fungi, protozoa, and viruses. Actinobacteria, Bacteroidetes, Firmicutes, and Proteobacteria are probably most significant for oral health.

Endogenous and exogenous factors affecting oral microbiota:

In healthy individuals, oral microbiome balance is regarded as dynamic because it changes in response to endogenous and exogenous factors. Human lifestyle and experiences can quickly and profoundly change the stability of microbial communities associated with the host.⁵ In other words, host lifestyle, physiology, genotype, pathobiology, environment, immune system, transient community members, and socioeconomic status are generally considered as important factors in the multifactorial background of oral diseases and systemic diseases.

Diets:

The change of dietary macronutrients and diet type can lead to a shift of the oral microbiome and diseases. Nutrients, such as sugars, fats and vitamins, play important roles in the oral microbiome. In severe early childhood caries, sugar-rich diets and frequent snacks show the highest associations with *Streptococcus mutans* (*S. mutans*) and *Fusobacterium nucleatum* (*F. nucleatum*).

Drinking:

The influence of red liquor and wine on the oral microbiota is different. Liquor could lead to an increase in the concentration and number of gram-positive bacteria, such as *S. mutans*. Oral bacteria convert ethanol to acetaldehyde, which is a toxin and recognized human carcinogen⁽²⁾.

Oral bacteria and systemic diseases:

Increasingly, evidence suggests that specific bacterial infections promote development of certain diseases. Accordingly, this section mainly summarizes the relationships between oral bacteria and systemic diseases. It also provides a deep insight into the mechanistic role in the influence of oral microbiota on cancers and inflammatory diseases^(3,4).

Oral bacteria and cancers

Oesophageal cancer

Oesophageal cancer is the eighth most frequent tumour and sixth leading cause of cancer death worldwide.⁵⁵ The latest study showed that oral bacteria might increase the risk of oesophageal cancer. Immunohistochemically, *Porphyromonas gingivalis* (*P. gingivalis*) has been detected in 61% of cancerous tissues, 12% of adjacent tissues, and 0% of normal oesophageal mucosa⁽⁵⁾.

Colorectal cancer:

Fusobacteria, which are from the mouth, cause excessive immune responses and turn on cancer growth genes. The microbes have been linked with colorectal cancer.⁵⁷ Fusobacteria gather massively in adenomas – a benign bowel growth that will become cancerous as time goes on. The polymicrobial nature of oral biofilms and the asaccharolytic metabolism of many of these species helps them live well in the microenvironment of colonic lesions.⁵⁸ By attracting special immune cells, fusobacteria invade the bowel and set off an inflammatory response that could accelerate the formation of colorectal tumours. Fusobacteria have specific surface molecules assisting them to attach and invade human colorectal cancer cells. In colorectal cancer, *F. nucleatum* has been demonstrated to expand myeloid-derived immune cells, strongly inhibit T-cell proliferation or activation, and induce T-cell apoptosis^(5,6).

Oral bacteria and inflammatory diseases

Atherosclerosis

Accurate and early diagnosis of cardiovascular diseases will greatly improve the survival rate of patients. Oral microbiota such as *S. mutans*, *P. gingivalis*, and *Gomella hemolysin* (*G. hemolysin*) may play a role in cardiovascular disease.

S. mutans could contribute directly to atherosclerosis by disrupting endothelial cell function, one of the earliest indicators of cardiovascular diseases. *S. mutans* is a major pathogen for dental caries. Oral *S. mutans* induced intracerebral hemorrhage experimentally and affected cerebral microbleeds. A significant correlation of *cnm*-positive *S. mutans* was observed with hypertensive intracerebral hemorrhage and deep cerebral microbleeds^(5,6).

Pneumonia

Aspiration of bacteria from the oral cavity into the lower airway was possible since the surfaces of oral cavity were contiguous with those of the trachea and lower airway. Oral bacteria continuously flowed into the lungs, and the lungs exhausted the bacteria through ciliary actions and coughing. The lungs are constantly exposed to diverse communities of microbes from the oropharynx, and novel culture-independent techniques of microbial identification have revealed that the lungs, previously considered sterile in health, harbor diverse communities of microbes^(5,6).

Heart diseases:

Five oral commensal bacteria (*Campylobacter rectus*, *P. gingivalis*, *Porphyromonas endodontalis*, *P. intermedia*, *Prevotella nigrescens*) were unique to coronary artery disease when compared with several non-cardiac disorders.⁷⁸ And the presence of *A. actinomycetemcomitans* in the subgingival area was associated with an almost twofold risk of angiographically confirmed stable CAD^(5,6).

Rheumatoid arthritis:

Rheumatoid arthritis (RA) is a systemic, inflammatory autoimmune disease. Most clinical studies involving specific oral microorganisms as triggers for RA were only dependent on serological detection methods. Rheumatoid factors had been identified as autoantibodies that reacted to the IgG molecule in the Fc region, and these antibodies could be the IgM, A, G or E epitopes. *P. gingivalis* proteinase was responsible for the epitope development in the RF Fc region. A previous study identified the lysine and arginine amino acid sequences for the Fc region of the IgG molecule; because *P. gingivalis* specifically decomposed lysine and arginine, the IgG3 CH2 and CH3 domains processed by *P. gingivalis* proteinase became powerful targets for the RF produced by rheumatoid cells^(5,6).

CONCLUSION:

Oral microbiota is an important intermediate link, causing different oral and overall health in the body under the influence of changes in a variety of factors. Once the microbiota balance has been disturbed, it may result in oral and even systemic diseases. Although a number of causes including infectious pathogens or use of antibiotics can lead to a disruption of microbial equilibrium, the role of our diet, nutrition, lifestyle and socioeconomic status is crucial.

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